FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

ATTY. DOCKET NO .:

065435-9014

Sheet 1 of 5

SERIAL NO.:

10/069,202

Thurston et al.

APPLICANT: FILING DATE:

February 22, 2002

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|---------------------|---|--------------------|-------------|------------------|-------|----------|----------------------------------|
| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
| BIK. | 1 | 3,523,941 | 11 Aug 1970 | Leimgruber et al | 260 | 239.3 | • |
| [| 2 | 3,524,849 | 18 Aug 1970 | Batcho et al | 260 | 239.3 | |
| | 3 | 4,239,683 | 16 Dec 1980 | Takanabe et al | 260 | 239.3 | |
| | 4 | 4,309,437 | 05 Jan 1982 | Ueda et al | 424 | 274 | |
| | 5 | 5,143,854 | 01 Sep 1992 | Pirrung et al | 436 | 518 | |
| * | 6 | 5,545,568 | 13 Aug 1996 | Ellman | 436 | 518 | |

FOREIGN PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION YES NO |
|---------------------|----|--------------------|--------------|---------------|----------|----------|-----------------------|
| D.K. | 7 | 1 299 198 | 06 Dec 1972 | Great Britain | <u> </u> | | |
| 1 | 8 | 2 586 683 | 06 Mar 1987 | France | | | X |
| | 9 | WO 88/04659 | 30 June 1988 | PCT/US | | | |
| | 10 | WO 91/16324 | 31 Oct 1991 | PCT/US | | | |
| | 11 | WO 92/19620 | 12 Nov 1992 | PCT/FR | | | X |
| | 12 | WO 96/23947 | 08 Aug 1996 | PCT/US | | | |
| | 13 | WO 97/01560 | 16 Jan 1997 | PCT/US | | | |
| | 14 | WO 97/07097 | 27 Feb 1997 | PCT/NZ | | | |
| | 15 | WO 98/11101 | 19 Mar 1998 | PCT/NZ | | | |
| | 16 | WO 99/29642 | 17 Jun 1999 | PCT/US | | | |
| | 17 | WO 00/12506 | 09 Mar 2000 | PCT/GB | | | |
| | 18 | 57-131791 | 14 Aug 1982 | Japan | | | X |
| $\overline{\nu}$ | 19 | 58180487 A | 21 Oct 1983 | Japan | | | X |

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

| N.V. | 20 | Althuis, T.H. et al., "Synthesis and identification of the major metabolites of Prazosin |
|------|----|---|
| N K | | formed in dog and rat," 20:1, 146-149 (1977). |
| 1 | 21 | Aristoff, P.A. et al., "Synthesis of CBI-PDE-I-Dimer, the benzannelated analogue of CC- |
| | | 1065," J.Org.Chem.," 57, 6234-6239 (1992). |
| | 22 | Aristoff, P.A. et al., "Synthesis of biochemical evaluation of the CBI-PDE-I-dimer, a benzannelated |
| - 1 | | analog of (+)-CC-1065 that also produces delayed toxicity in mice," J.Med.Chem., 36, 1956-1963 |
| | | (1993). |
| | 23 | Baraldi, P.G. et al., "Design, synthesis and biological activity of a pyrrolo [2,1-c][1,4] |
| | | benzodiazepine (PBD)-distamycin hybrid," Bioorg. Med. Chem. Ltrs., 8, 3019-3024 (1998). |
| 1 | 24 | Bi, Y. et al, "Building blocks for peptide and carbamate libraries," Bioorg. Med. Chem. |
| | | Ltrs, 6:19, 2299-2300 (1996). |
| V | 25 | Bi, Y., et al, "Building blocks for peptide and carbamate libraries," Chemical Abstracts, |
| • | | 300965y, 125:23, p.1013 (1996). |
| | | |

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



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065435-9014

Sheet 2 of 5

SERIAL NO.:

10/069,202

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Thurston et al.

FILING DATE:

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GROUP:

1624

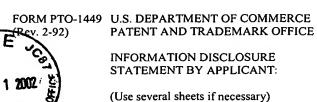
| B.K. | 26 | Boger, D.L., "Design, synthesis, and evaluation of DNA minor groove binding agents: the |
|------|----------|--|
| 1)/ | <u> </u> | duocarmycins," Pure & Appl. Chem., 66:4, 837-844 (1994). |
| 1 | 27 | Boger, D.L. et al., "Total synthesis and evaluation of ±-N-(tert-butyloxycarbonyl)-CBI (±)-CBI-CDPI ₁ and (±)-CBI-CDPI ₂ CC-1065 functional agents incorporating the equivalent 1,2,9,9a-tetrahydrocycloprop[1,2-c]benz[1,2-e]indol-4-one(CBI) left-hand subunit," J. Am. Chem Soc., |
| | | 111:16, 6461-6463 (1989). |
| | 28 | Boger, D.L. et al., "Synthesis of N-(tert-butyloxycarbonyl)-CBI,CBI,CBI-CDPI ₁ , and CBI-CDPI ₂ : Enhanced functional analogues of CC-1065 incorporating the 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) left-hand subunit,". Org. Chem., 55:23, 5823-5832 (1990). |
| | 29 | Boger, D.L. et al., "An efficient synthesis of 1,2,9,9a-tetrahydrocyclopropa[c]benz[e] indol-4-one (CBI): An enhanced and simplified analog of the CC-1065 and duocarmycin alkylation subunits," J. Org. Chem., 60:5, 1271-1275 (1995). |
| | 30 | Boger, D.L. et al., "CBI-TMI: Synthesis and evaluation of a key analog of the duocarmycins. Validation of a direct relationship between chemical solvolytic stability and cytotoxic potency and confirmation of the structural features responsible for the distinguishing behavior of enantiomeric paris of agents," J. Am. Chem. Soc., 116:18, 7996-8006 (1994). |
| | 31 | Boger, D.L. et al., "CC-1065 and the duocarmycins: synthetic studies," Chem. Rev., 97:3, 787-828 (1997). |
| | 32 | Bose, D.S et al., "New approaches to pyrrolo[2,1-c][1,4]benzodiazepines: synthesis, DNA-binding and cytotoxicity of DC-81," <i>Tetrahedron</i> , 48:4, 751-758 (1992). |
| | 33 | Bose, D.S. et al., "Rational design of a highly efficient irreversible DNA interstrand cross-linking agent based on the pyrrolobenzodiazepine ring system," J. am. Chem. Soc., 114:12, 4939-4941 (1992). |
| | 34 | Brown, S.C. et al., "NMR solution structure of a peptide nucleic acid complexed with RNA," Science, 265, 777-780 (1994). |
| | 35 | Burgess, K. et al., "Solid phase syntheses of oligoureas," J. Am. Chem. Soc., 119:7, 1556-1564 (1997). |
| | 36 | Burgess, K. et al., "Solid-phase syntheses of unnatural biopolymers containing repeating urea units," Agnew. Chem. Int. Ed. Engl., 34:8, 907-909 (1995). |
| | 37 | Cava, M.P. & Drost, K.J., "A photochemically based synthesis of the benzannelated analogue of the CC-1065 A unit," <i>J. Org. Chem.</i> , 56:6, 2240-2244 (1991). |
| | 38 | Cho, C.Y. et al., "An unnatural biopolymer," Science, 261, 1303-1305 (1993). |
| | 39 | Courtney, S.M. et al., "A new convenient procedure for the synthesis of pyrrolo[2,1-c][1,4]benzodiazepines," <i>Tetrahedron Ltrs.</i> , 34:33, 5327-5328 (1993). |
| | 40 | Edman, P. et al., "A protein sequenator," European J. Biochem., 1:1, 80-91 (1967). |
| | 41 | Egholm, M. et al, "Peptide nucleic acids (PNA). Oligonucleotide analogues with an achiral peptide backbone," J. Am. Chem. Soc., 114, 1895-1897 (1992). |
| | 42 | Egholm, M. et al., "PNA hybridizes to complementary oligonucleotides obeying the Watson-Crick hydrogen-bonding rules," <i>Nature</i> , 365, 566-568 (1993). |
| | 43 | Farmer, J.D., Jr. et al., "DNA binding properties of a new class of linked anthramycin analogs," <i>Chemical Abstract</i> , 239940r, 114:25, p.25 (1991). |

EXAMINER

Bruch Zill

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



ATTY. DOCKET NO.:

065435-9014

Sheet 3 of 5

SERIAL NO.:

10/069,202

0/069,202

Thurston et al.

APPLICANT:

February 22, 2002

GROUP:

FILING DATE:

1624

| | 1 4 4 | The state of the s |
|--------------|----------|--|
| B.K. | 44 | Figliozzi, G.M. et al., "Synthesis of N-substituted glycine peptoid libraries," Methods |
| <i>V</i> / · | <u> </u> | in Enzymology, 267:25 437-47 (1996). |
| 1 | 45 | Foloppe, M.P. et al., "DNA-binding properties of pyrrolo[2,1-c][1,4]-benzodiazepine |
| | | N10-C11 amidines," Eur. J. Med. Chem., 31, 407-410 (1996). |
| 1 | 46 | Fujisawa Pharm., "Benzodiazepine derivatives," Chemical Abstracts, 139983k, 99:17 |
| | L | 603 (1983). |
| | 47 | Fujisawa Pharm., "Benzodiazepine derivatives," Chemical Abstracts, 72145x, 98:9, |
| - 1 | | 638 (1983). |
| | 48 | Fukuyama, T. et al., "Total synthesis of (+)-porothramycin B," Tetrahedron Ltrs., |
| ı | | 34:16, 2577-80 (1993). |
| | 49 | Furka, A. et al., "General method for rapid synthesis of multicomponent peptide |
| 1 | '- | mixtures," In. J. Peptide Protein Res., 37 487-493 (1991). |
| | 50 | Gregson, S.J. et al., "Synthesis of a novel C2/C2'-exo unsaturated |
| 1 |] 30 | pyrrolobenzodiazepine cross-linking agent with remarkable DNA binding affinity and |
| 1 | | cytotoxicity," Chem. Commun., 797-798 (1999). |
| | 51 | Guiotto, A. et al., "Synthesis of novel C7-aryl substituted pyrrolo[2,1- |
| - 1 | 31 | |
| | 1 | c][1,4]benzodiazepines (PBDs) via pro-N10-troc protection and suzuki coupling," |
| | 52 | Bioorg. Med. Chem. Ltrs., 8:21, 3017-3018 (1998). |
| 1 | 52 | Hara, M. et al., "A new glycosidic pyrrolo[1,4]benzodiazepine antibiotic produced by |
| | | streptomyces sp." J. Antibiotics, 41:5, 702-704 (1988). |
| | 53 | Hochlowski, J.E. et al., "Abbeymycin, a new anthramycin-type antibiotic produced by |
| | | a streptomycete," J. of Antibiotics, 40:2, 145-148 (1987). |
| 1 | 54 | Hurley, L.H. et al., "Covalent binding of antitumor antibiotics in the minor groove of |
| | | DNA. Mechanism of action of CC-1065 and the pyrrolo[1,4]benzodiazepines," Acc. |
| | | Chem. Res., 19, 230-237 (1986). |
| | 55 | Itoh, J. et al., "Sibanomicin, a new pyrrolo[1,4]benzodiazepine antitumor antibiotic |
| | | produced by a micromonospora sp.," J. Antibiotics, 41:9,1280-1284 (1988). |
| | 56 | Jenkins, T.C. et al., "Structure of a covalent DNA minor groove adduct with a |
| ļ | | pyrrolobenzodiazepine dimer: Evidence for sequence-specific interstrand cross- |
| 1 | | linking," J. Med. Chem., 37:26, 4529-4537 (1994). |
| \top | 57 | Kohn, K.W., "Anthramycin," Antibiotics, III, 3-11 (1975). |
| | 58 | Konishi, M. et al., "Chicamycin, a new antitumor antibiotic II. Structure |
| | | determination of chicamycins A and B," J. Antibiotics, 37:3, 200-206 (1984). |
| | 59 | Kunimoto, S. et al., "Mazethramycin, a new member of anthramycin group |
| 1 | | antibiotics," J. Antibiotics, 33:6, 665-667 (1980). |
| 1 | 60 | Langley, D.R. et al., "A versatile and efficient synthesis of carbinolamine-containing |
| 1 | | pyrrolo[1,4]benzodiazepines via the cyclization of N-(2-aminobenzoyl)pyrrolidine- |
| \ | | 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 |
| | | 52:1, 91-97 (1987). |
| + | 61 | Leber, J.D. et al., "A revised structure for sibiromycin," J. Am. Chem. Soc., 110:9, |
|]/ | 01 | 2992-2993 (1988). |
| NI/ | ı | 4774 - 4773 (1700). |

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Sheet 4 of 5

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SERIAL NO.:

10/069,202

Thurston et al.

FILING DATE:

APPLICANT:

February 22, 2002

GROUP:

1624

| 62 Leimgruber, M. et al., "The structure of anthramycin," J. Am. Chem. Soc., 8 5793-5795 (1965). 63 Leimbruger, M. et al., "Isolation and characterization of anthramycin, a new antitumor antibiotic," J. Am. Chem. Soc., 87:24, 5791-5793 (1965). 64 Lescrinier, T. et al., "DNA-binding ligands from peptide libraries containing unnatural amino acids," Chem. Eur. J., 4:3, 425-433 (1998). 65 Lown, J.W. et al., "Antitumor antibiotics," Biochem. Pharmacol., 28:13, 20 (1979). | g 17-2026 |
|---|------------------------|
| antitumor antibiotic," J. Am. Chem. Soc., 87:24, 5791-5793 (1965). 64 Lescrinier, T. et al., "DNA-binding ligands from peptide libraries containing unnatural amino acids," Chem. Eur. J., 4:3, 425-433 (1998). 65 Lown, J.W. et al., "Antitumor antibiotics," Biochem. Pharmacol., 28:13, 20 | g 17-2026 |
| Lescrinier, T. et al., "DNA-binding ligands from peptide libraries containing unnatural amino acids," Chem. Eur. J., 4:3, 425-433 (1998). Lown, J.W. et al., "Antitumor antibiotics," Biochem. Pharmacol., 28:13, 20 | 17-2026 |
| 65 Lown, J.W. et al., "Antitumor antibiotics," Biochem. Pharmacol., 28:13, 20 | |
| | liverse |
| Monks, A. et al., "Feasibility of a high-flux anticancer drug screen using a depanel of cultured human tumor cell lines," J. of Nat'l Cancer Inst., 83:11, 75 (1991). | |
| 67 Moran, E.J. et al., "Novel biopolymers for drug discovery," Peptide Science 219 (1995). | 2, 37, 213- |
| 68 Nagasaka, T. et al., "Stereoselective synthesis of tilivalline," Tetrahedron Logistics 30:14, 1871-1872 (1989). | etters, |
| 69 Nagasaka, T. et al., "Stereoselective synthesis of tilivalline," J. Org. Chem., 6797-6801 (1998). | 63:20, |
| 70 Nielsen, P.E. et al., "Sequence-selective recognition of DNA by strand disple with a thymine-substituted polyamide," Science, 254, 1497-1500 (1991). | acement |
| 71 O'Neil, Ian <i>et al.</i> , "The synthesis of functionalized pyrrolo[2,1-e][1,4]-benzodiazepines," <i>Chemical Abstracts</i> , 126:13, 618 (1997) and entire article | |
| 72 O'Neil, Ian A. et al., "DPPE: A convenient replacement for triphenylphosp Staudinger and Mitsunobu reactions," <i>Tetrahedron Letters</i> , 39:42, 7787-779 | hine in the 00 (1998). |
| 73 Paikoff, S.J. et al., "The solid phase synthesis of N-alkylcarbamate oligomen Tetrahedron Letters, 37:32, 5653-5656 (1996). | rs," |
| Rawal, V.H. <i>et al.</i> , "Photocyclization strategy for the synthesis of antitumor CC-1065: Synthesis of dideoxy PDE-I and PDE-II. Synthesis of Thiophene analogues of dideoxy PDE-I and PDE-II, <i>J. Org. Chem.</i> , 52:1, 19-28 (1987). | and Furan |
| 75 Reynolds, V.L. <i>et al.</i> , "The chemistry, mechanism of action and biological p of CC-1065, a potent antitumor antibiotic," <i>J. Antibiotics</i> , 39:3, 319-334 (19 | properties |
| Saha, A.K. <i>et al.</i> , "Diisopropylsilyl-linked oligonucleotide analogs: Solid-ph synthesis and physicochemical properties," <i>J. Org. Chem.</i> , 58:27, 7827-7831 | nase |
| 77 Schreiber, S.L., Kapoor, T.M. <i>et al.</i> , "Exploring the specificity pockets of two homologous SH3 domains using structure-based, split-pool synthesis and aftibased selection," <i>J. Am. Chem. Soc.</i> , 120:1, 23-29 (1998). | |
| 78 Shimizu, K. et al., "Prothracarcin, a novel antitumor antibiotic," J. Antibiotic 972-978 (1982). | cs, 35:8, |
| 79 Simon, R.J. et al., "Peptoids: A modular approach to drug discovery," Proc. Acad. Sci. USA, 89, 9367-9371 (1992). | . Natl. |
| Soth, M.J. et al., "Unnatural oligomers and unnatural oligomer libraries," Ci Chem. Biol., 1:1, 120-129 (1997). | ırr. Opin. |

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Sheet 5 of 5

10/069,202

Thurston et al.

February 22, 2002

GROUP:

SERIAL NO.:

APPLICANT:

FILING DATE:

1624

| D.K. | 81 | Takeuchi, T. et al., "Neothramycins A and B, new antitumor antibiotics," J. Antibiotics, 29:1, 93-96 (1976). |
|------|----|---|
| | 82 | Thurston, D.E. et al., "Synthesis of DNA-interactive pyrrolo[2,1-c][1,4]benzodiazepines," Chem. Rev. 94:2, 433-465 (1994). |
| | 83 | Thurston, D.E. et al., "The molecular recognition of DNA," Chem. Britain, 26, 767-772 (1990). |
| | 84 | Thurston, D.E. et al., "Synthesis of a novel GC-specific covalent-binding DNA affinity-cleavage agent based on pyrrolobenzodiazepines (PBDs)," Chem. Commun., 563-565 (1996). |
| | 85 | Thurston, D.E., "Advances in the study of pyrrolo[2,1-c][1,4]benzodiazepine (PBD) antitumour antibiotics," <i>Molecular Aspects of Anticancer Drug-DNA Interaction</i> , Neidle, S., Waring, M.J., Eds.; Macmillan Press Ltd., v.1, 54-88 (1993). |
| | 86 | Thurston, D.E. et al., "Effect of A-ring modifications on the DNA-binding behavior and cytotoxicity of pyrrolo[2,1-c],[1,4]benzodiazepines," J. Med. Chem. 42:11, 1951-1964 (1999). |
| | 87 | Tsunakawa, M. et al., "Porothramycin, a new antibiotic of the anthramycin group: production, isolation, structure and biological activity," J. Antibiotics, 41:10, 1366-1373 (1988). |
| | 88 | Umezawa, H. et al., "Mazethramycins," Chemical Abstracts, 90:1, 428 (1979). |
| | 89 | Wilson, S.C. <i>et al.</i> , "Design and Synthesis of a novel epoxide-containing pyrrolo[2,1-c][1,4]benzodiazepine (PBD) via a new cyclization procedure," <i>Tetrahedron Ltrs.</i> , 36:35, 6333-6336 (1995). |
| | 90 | Zuckermann, R.N. et al., "Discovery of nanomolar ligands for 7-transmembrane G-protein-coupled receptors from a diverse N-(substituted)blycine peptoid library," J. Med. Chem., 37:17, 2678-2685 (1994). |

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EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.